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Herbicide Resistance in Plants

92

The first discovery of a triazine-resistant weed (common ground-sel) was in western Washington in the late 1960s. The subsequent widespread and frequent occurrence of other triazine-resistant weeds over the past 20 years have made triazine herbicide-resistance the best known and most studied case of herbicide-resistance. Triazine-resistance has also been of great interest because of the importance and extensive use of this group of herbicides. If other single target site residual herbicides (e.g., diuron) were used as extensively and continuously as the triazines, they would have almost certainly led to resistant biotypes.

Although weeds have taken longer to evolve herbicide-resistance compared to insect pests and pathogens, biotypes of 40 broadleaves and 15 grass weed species are known to have developed resistance to triazine herbicides somewhere in the world. A total of 45 weed biotypes (29 broadleaves and 16 grasses) have evolved resistance to 14 other types of classes of herbicides, making a grand total of 100 herbicide-resistant weed biotypes to date. Only 21 of the triazine-resistant biotypes and 16 biotypes resistant to other herbicides have been found in the U.S., but one or more of these resistant biotypes have invaded 39 states, six provinces of Canada and 27 other countries.

LeBaron noted that this paper was represented as the President of the Weed Science Society of American and as a weed scientist, rather than a representative of CIBA-GEIGY Corporation.

Past experience has shown that weeds resistant to triazines can be managed or restrained within a reasonable limit. In the U.S. the total area of land or crops infested with triazine-resistant weeds is still relatively limited (estimated to be about 3,000,000 acres) and does not seem to be expanding rapidly, except in a few states where continuous corn or no-tillage farming is being practiced or good alternative herbicides are not used. In most areas of the U.S. where triazine-resistant weeds have evolved it has not even been necessary or desirable to cease using the triazine herbicide of choice, due to the many susceptible weeds that are still usually prevalent. In a few cases, the resistant biotypes have even disappeared.

It is very important for nonbiologists to understand that an essential requirement of herbicides is that they control all weeds throughout the season. This may be from 5 to 25 species, not just the one or two pests that insecticides and fungicides usually try to control. If all but one species is controlled, little has been accomplished because that species will take over. This also makes it difficult for weed scientists to deal with weed thresholds because if the "escapes" are resistant to the herbicide used, within one or two years the field will likely be a solid stand of resistant weeds. Even if they are susceptible escapes, many weeds tend to expand to fill up the space available, which again is different from insect and disease pests. Most herbicides must also have some soil persistence in order to control weeds that germinate later in the season.

93

Over the 45 years that modern herbicides have been developed and used extensively, there have been many cases of differential tolerance within various weed species, such as intraspecific resistance to 2, 4-D, Dalapon®, and other herbicides. There are seen many examples of evolution toward interspecific herbicide tolerance. Researchers who have been trying to control weeds for some time have learned in many ways that nature is neither an exact nor fixed science. Nothing remains constant and weeds have been around a lot longer than scientists have. Weeds have learned to adapt and evolve to survive.

Some of the modern chemical tools have been so spectacular compared to the cultivator and hoe that we have become accustomed to seeing clean, weed-free fields, and become a bit complacent. Even when triazine resistance evolved, an easy way to circumvent these interlopers was found, with a new generation of spectacular herbicides

(e.g., sulfonylureas, imidazilones) which are effective at grams per acre instead of pounds per acre. They are just what was needed to help solve environmental concerns and other problems while adding dimension and flexibility to our weed control technology. Again weed scientists marveled at the success and potential of their inventions, but did not look back to see what nature was doing. Within the past few years, an increasing number of weeds have evolved resistance to these and several other new types of herbicides.

NEW ROLE OF HERBICIDE-RESISTANT CROPS

94 Knowledge about herbicide sites and modes of action has been essential in the research and understanding of herbicide-resistance mechanisms. Herbicide-resistant weeds have also been valuable scientific tools, contributing greatly to the understanding of herbicide modes of action, plant biochemical and physiological processes, molecular genetics, physical structure, and anatomy. However, it is interesting and significant that the mechanisms of resistance developed by weeds are often different from the mechanisms of selectivity to those herbicides in most crops. This is certainly true with the most prevalent and thoroughly studied cases of herbicide-resistance, including the triazines, dinitroanilines, and acetolactate synthetase (ALS) inhibitors.

For example, in the goosegrass (*Eleusine indica*), weed biotyped resistance to trifluralin, the tubulin in the roots, is apparently altered so that dinitroaniline herbicides are not effective in preventing tubulin polymerization into microtubules, which is assumed to be the mechanism of action of these herbicides. However, selectivity in most crops to these herbicides is believed to be due to the ability of their tap roots to rapidly grow through the treated soil layer or differential lipid content in seeds, thereby avoiding significant herbicide exposure.

Resistance mechanisms in weed biotypes to ALS inhibitors are apparently due to an alteration in the gene coding for acetolactate synthetase, resulting in various forms of insensitive ALS enzymes, the main target site of these herbicides. Crop tolerance, however, seems to be mostly dependent on differential metabolism.

Research to date indicates that most of the triazine-resistant biotypes lack the normal triazine binding sites in their chloroplasts, whereas crop selectivity is due mainly to metabolism or translocation differences. Triazine-resistant velvetleaf (*Abutilon theophrastis*) in Maryland is an exception in that resistance is due to enhanced glutathione transferase activity.

While most crops and weeds are susceptible to paraquat, paraquat-resistant horseweed (*Conyza*) biotypes may be insensitive to the herbicide due to elevated levels of superoxide dismutase and other enzymes, or to differential binding or distribution of the herbicide in the weed.

Recent research on the physiological basis of mecoprop resistance in chickweed indicated that resistance is due to reduced mecoprop binding at the sites of action in resistant plants. Data on mechanisms of most other types of herbicide-resistance in weeds are still not complete.

RESISTANT WEEDS AND CROPS AND THE FUTURE OF HERBICIDES

Resistance to the ALS inhibitors and other newer herbicides has already become a very serious issue. Industry, especially Du Pont, has responded quickly and appropriately to completely modify their marketing strategy and research programs to manage potential weed resistance to their sulfonylureas. Such responsible reaction of the part of the industry must be encouraged and supported. Everyone connected with agriculture should view herbicides as important nonexpendable tools that must be preserved for future generations. It is gratifying to hear and see more about product stewardship than ever in the past. Past performance in pest resistance management and use of our insecticides and fungicides, both in industry and on the farm, has often been irresponsible and shameful, and has contributed much to a poor public image. There must be better in management of herbicides and resistant weeds.

95

Of special concern is the occurrence of cross-resistance to many herbicides within the same species. The few cases to date are still a long distance away. The most noted examples are *Lolium rigidum* (annual ryegrass) in Australia and *Alopecurus* (blackgrass) in the U.K. However, it is very worrisome that multiple cross-resistance to herbicides can occur in plants, apparently by similar mechanisms (metabolic detoxification, e.g., mixed function oxidases) to some insects which rapidly evolve resistance to insecticides. Such efficient oxidation of foreign organic chemicals may prevent almost any herbicide from reaching the target site intact. When I first saw the one known case of diclofop methyl resistant ryegrass in Australia about three and a half years ago, and I learned that it was cross-resistant to most sulfonylureas, I warned them that they were potentially facing the worst

case of herbicide-resistance I knew of in the entire world. This has proven to be the case, as this multiple-resistant weed has become widespread throughout most of the cereal producing areas of Australia. The solutions to this problem will not be easy, and cultural and agronomic methods will have to be included as well as, or possibly in place of chemical methods. Because of the striking ability this weed has for developing resistance to many herbicides, not only in Australia but in other parts of the world, *Lolium* is the housefly or Colorado potato beetle of the plant kingdom. A diclofop methyl-resistant *Lolium multiflorum* (Italian ryegrass) was recently discovered in Oregon. It was found to have some degree of cross-resistance. This genus must be respected, and we must avoid in any way possible evolving such plants with multiple resistant potential.

96

Because of much lower application rates, with less perceived human, animal and environmental exposure and risks, a very strong perception exists among government agencies and policymakers that the new sulfonylurea herbicides will replace many of those in current use. This perception comes at a time when some of the earlier herbicides are being discontinued or are in trouble because of economics, reregistration requirements, toxicology and environmental concerns. There will be a great need for the older herbicides and other tools of agricultural technology in the future. Chemical herbicides must be a major part of the agricultural technology in the decades ahead to provide the constantly greater demand for food, fiber and shelter, with greater cost effectiveness. But other means of pest control must not be discarded, nor should there be too much dependence on chemicals alone. Herbicide-resistance is acting as a self-imposed limiting system of nature, and nature sets the rules—be flexible or lose.

With the first invasion of resistant weeds, prompt action is essential in order to avoid serious and more permanent problems. Preventive action to avoid herbicide-resistant weeds from developing in the first place is definitely the best strategy. It is virtually essential in all cases of herbicide-resistance to have other classes or types of herbicides, with alternate sites and mode of action, available. In some countries and situations, control of triazine-resistant weeds has not been successful, resulting in rapid invasion and almost total loss of these herbicides in the area.

I have great concerns and doubts whether we can be as successful in avoiding or managing the more recent resistant biotypes as we have been with triazine-resistant weeds in the past. Not only are herbicide-resistant weeds appearing after fewer repeat annual applications of some of the newer herbicides, but there seems to be some species that have potential for resistance. It is likely that many, if not all, weeds possess some ability to evolve resistance to these herbicides. In addition, the resistant biotypes are apparently equally fit and competitive once they evolve, unlike most biotypes resistant to triazine herbicides.

Both wisdom and understanding developed on pest resistance to pesticides must be utilized, as well as greater marketing control and self-restraint than has thus far been demonstrated in U.S. agriculture, must be exercised in order to protect or prolong the use of the sulfonylurea and other herbicides with a single site of action and high risk for resistance. The following changes or strategy rules will be required:

- These herbicides should be marketed only in combinations, especially in major crops, if other types of herbicides are available as suitable partners.
- Crop and herbicide rotations should be used whenever possible. In rotations, avoid those with the same weed spectra.
- Use of long residual ALS herbicides should be avoided or minimized.
- Use the lowest rates possible.
- Minimize the number of applications per season, and use only every two or three years.
- Education and cooperation of industry management, marketing, sales, extension, farmers, and others is essential.
- Government agencies and policymakers must realize that all possible herbicides must be retained as potential mixing partners.
- Industry should not develop and market ALS resistant crops or crops resistant to only one herbicide with a high risk for resistance for the purpose of greatly expanding their use. This approach should be used to enhance tolerance in crop varieties, to avoid carry-over injury, for specific and limited special problems, and for minor acreage and high value crops. A major objective of developing herbicide-resistant crops should be to provide more flexibility in control of resistant weeds.

—These herbicides should be used in crops only where several other good mixing partners, cultivation, and other weed control options are available.

—Cultivators or other mechanical weed control options should remain available. Conservation tillage systems may not be a long-term or continuing option.

—If possible, industry should continue to develop chemicals in this class that will inhibit all types of ALS enzymes and overcome this resistance.

—Develop other herbicides that do not have a single site of action and are not as likely to induce resistance.

—Lastly, do not throw away the hoe, but rogue out the weeds that escape if resistance occurs or is suspected, or use systems that preferentially control resistant weeds.

98

Many politicians and those who like to tell farmers how to farm mention that herbicide-resistant weeds are one more reason for abandoning herbicides in favor of other methods. This is fine if other methods are actually available, profitable and environmentally desirable. But resistant weeds require that all possible herbicides be retained so that farmers have all possible options. Nature plays no favorites. Weeds, as with insects and diseases, will tend to survive and evolve resistance to any method used to control them.

I can agree with proponents of sustainable agriculture that we have at times depended on herbicides too much, or have expected too much from them. However, we should not ask farmers to get by without herbicides, and no one who likes to eat should try to compel them to do so. Rather, we must learn to better manage herbicides and preserve them by learning to use them as essential tools while avoiding and managing resistant weeds. We must also make further scientific breakthroughs or improvements in formulations, application technology, and handling methods to reduce human and environmental exposure and risk. These new low-rate herbicides must continue to be an important part of our future defense against weeds.

There is no way that biological and other nonchemical methods of weed control will totally replace chemicals in our lifetime. If anything has been learned in the past 40 years, it is that we will need all the help

we can get to keep ahead of the pests, and to depend on only one tool or method against major pests is a sure road to failure and scientific heresy. Chemicals will continue to be essential and the main line of defense against weeds, and will help to produce the crops and pay for the research on biological controls, biotechnology, and sustainable agriculture while other tools are being developed.

As implied above, genetic engineers should reevaluate their strategy in developing herbicide-resistant crops. Five years ago, there were over 100 scientists or laboratories working on triazine resistant crops. This interest has greatly decreased for a number of valid reasons. The shift in priority has been toward ALS inhibitors and glyphosate. To scientists who are working on such a project for the purpose of using one of these specific herbicides exclusively and continuously, I strongly recommend that you drop the effort. Not only will it take longer to get the crop ready and approved for commercial introduction than originally planned, and resistant weeds may have already invaded your market, but if your herbicide of choice is used repeatedly, it will likely be only a few years before it will have resistance problems.

99

On the other hand, scientists should continue developing herbicide-resistant crops with the objective of offering growers greater weed control options and flexibility in the types of herbicides that can be used, especially as a strategy to control herbicide-resistant weeds. This research effort could also be justified by enhancing the natural selectivity of the target crop or reducing potential carry-over injury to rotational crops.

Most biotechnologists justified the need for genetically engineered crops as a way to get rid of pesticides. Now with the same kind of registration requirements and scrutiny that chemicals have always been subjected to required, biotechnologists are appalled at the confrontations and opposition. We need to be honest with each other and recognize that not only are biotechnologists working with live organisms that can reproduce, but in most cases, they are considering replacing a chemical with a chemical. While there may be some benefits of plant development, confinement of the toxicants, human or environmental risk, etc. there could even be more hazard from natural pesticides in engineered plants versus those treated with synthetic chemicals, unless they do not remain in the edible part of the crop and the plant residue is handled as a hazardous waste. But my major concern is that the

farmer needs all the help and options available, and we should not consider that biotechnology and biocontrol are in competition or conflict with chemicals, nor immune from resistance. It may be that pests can soon evolve resistance to the "natural" chemical or method, as well as those externally applied.

HERBICIDES AND LISA

100 Herbicides have already made great contributions to low input and sustainable agriculture. The Low Input Sustainable Agriculture (LISA) philosophy promotes conservation tillage, as do all weed scientists. However, without herbicides, there would be little or no conservation tillage in most crops. Soil conservation programs, agricultural sustainability and production efficiency are, and will continue to be, absolutely dependent upon herbicides. This does not mean that mechanical (e.g., tillage, moving), biological (e.g., mycoherbicides, allelopathy, cover crops), and other tools are of no value. However, these methods will continue over the next 20 to 30 years, at least, to be very limited in application, even though their development and use needs encouragement wherever they fit the problem. There are many ways that herbicides can and are being used to protect and enhance the environment for use by humans, birds and animals, and in most cases, they will be safer and have less environmental impact than other weed control tools such as mechanical tillage, biological (live organism) controls, etc.

The switch from the moldboard plow and cultivator to conservation tillage systems makes us more dependent on herbicides, but the benefits more than compensate for the risks. This trend should be continued and increased where it can be advantageous to agriculture, as well as the environment. Conservation tillage not only protects 50 to 90 percent of essential topsoil that would otherwise be permanently lost by water and wind erosion, but it prevents much more than just inert soil moving into streams, rivers, lakes and air. This reduced erosion, combined with the erodable cropland that has been planted to grasslands or woodlands have already saved more than half a billion tons per year of top soil. Much more soil will be preserved if the projected 40 million acres (11 percent of total cropland) is set aside over the next two years and better herbicide programs could be developed to make farmers more confident that the weeds can be controlled without tillage. Some watershed studies in recent years have shown a reversal from major losses to net gain in soil. The Environmental Protection

Agency (EPA) and the public are increasingly concerned about pesticides in groundwater since analytical advances have allowed us to measure very low and often meaningless levels of synthetic chemicals in water, mostly traceable to point-source contamination. Virtually nothing is known about natural pollutants or mutagens that have been and may still be in drinking water. Some scientists need to study the effects of herbicides versus tillage practices on the movement of natural toxins (e.g., organics, inorganics, and microorganisms) into our water and air, including their potential mutagenic or health effects, identification, characterization, and quantification. Herbicides have had beneficial effects on water quality through conservation tillage; the whole picture needs to be seen.

Furthermore, it must not be assumed that LISA or alternate farming methods have no environmental impacts. They may, in fact, cause exposure to more toxic or objectional contaminants than do herbicides. For example, I would prefer to drink water coming off of or from under a field treated with herbicides and commercial fertilizers rather than a field treated with 10 to 20 tons per acre of cow manure. We do not know everything that manure contains, and it may be that very little of it reaches groundwater, but there could be contaminants in runoff water. We need to know what the effects and comparative risks are, and not assume that LISA is a safer way to farm than using synthetic chemicals. There is not, never has been, and never will be zero-risk agriculture or life.

Another concern about LISA, or any arbitrary reduction in the use of herbicides, is the phenomenon of biological changes with time. In many situations, the weed populations and pressure are not the same as 30 years ago. Where herbicides have been extensively used, some species have almost disappeared and the weed seed density in the soil is often much reduced. This is not obvious or easy to measure, especially to nonbiologists, because there are still many weed seedlings that germinate each spring. This phenomenon is even contributing to some of the short-term successes from cutting back on herbicides. But, the full effect of reducing or eliminating herbicides will not be seen the first year. Nature will adapt and take advantage of any niche available, and the weed infestations and species will likely get worse with time.

PUBLIC AND POLITICAL PERCEPTIONS

The main problem in agriculture today is not the technology, but public perceptions. There is no significant exposure or risk to human health or the environment from herbicides in food or groundwater; we are at serious risk of solving the wrong problem. Ignorance, fear and emotions must be replaced by education, reason and rational thought and action. There is the option of dropping herbicide use and purchasing only food produced without them, but we will not remain competitive in world agriculture. We will depend more and more on imported foods, our surpluses will disappear, we will have less control on the quality of our food, and the greatest agricultural technology in the world that is responsible for providing by far the highest quality and variety of food at the lowest prices that this country or any other has ever known, will be in jeopardy.

102

With considerable misgivings, I am prompted to say that what we most likely need in this country and some others in the developed world is to experience a little famine. It is only because of our surplus and efficient production without farmers always being the economic benefactors that we have such vocal opponents to herbicides. With only two percent of our population on the farm, our graneries and supermarkets full, and people who do not have an appreciation for how sensitive the balance is between feast and famine, some difficult choices lie ahead. We need to learn to live with herbicides and solve the right problems.

In summary, nothing will come out of biotechnology, biocontrol organisms, or other presently perceived and much talked about technology that will substantially replace chemicals for weed control in the foreseeable future (20 to 40 years). I hasten to add that there will be very useful tools and technology developed to help us do better in selecting the more acceptable herbicides, using lower rates, reduce the leaching and environmental impact of those used, getting more of them to their sites of action, improve the integration of other control methods for best management practices, use of biologicals for control of major or noxious weeds which cannot be adequately controlled with herbicides, and other improvements for the protection of both crops and the environment. But just do not try to do it without chemical herbicides or agriculture will fail to be competitive, profitable, sustainable, or environmentally sound.